



# The Effect of Perioperative Ketorolac on the Clinical Failure Rate of Meniscal Repair

## Citation

Proffen, Benedikt L., Jason H. Nielson, David Zurakowski, Lyle J. Micheli, Christine Curtis, and Martha M. Murray. 2014. "The Effect of Perioperative Ketorolac on the Clinical Failure Rate of Meniscal Repair." *Orthopaedic journal of sports medicine* 2 (5): <http://ojs.sagepub.com/content/2/5/2325967114529537.full>. doi:10.1177/2325967114529537. <http://dx.doi.org/10.1177/2325967114529537>.

## Published Version

doi:10.1177/2325967114529537

## Permanent link

<http://nrs.harvard.edu/urn-3:HUL.InstRepos:13454746>

## Terms of Use

This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at <http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA>

## Share Your Story

The Harvard community has made this article openly available.  
Please share how this access benefits you. [Submit a story](#).

[Accessibility](#)

Published in final edited form as:

*Orthop J Sports Med.* ; 2(5): . doi:10.1177/2325967114529537.

## The Effect of Perioperative Ketorolac on the Clinical Failure Rate of Meniscal Repair

Benedikt L. Proffen, MD\*, Jason H. Nielson, MD\*, David Zurakowski, PhD\*, Lyle J. Micheli, MD\*, Christine Curtis, MPH\*, and Martha M. Murray, MD\*<sup>†</sup>

Investigation performed at Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts, USA

\* Division of Sports Medicine, Department of Orthopaedic Surgery, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts, USA.

### Abstract

**Background**—There has been recent interest in the effect of nonsteroidal anti-inflammatory medications on musculoskeletal healing. No studies have yet addressed the effect of these medications on meniscal healing.

**Hypothesis**—The administration of ketorolac in the perioperative period will result in higher rates of meniscal repair clinical failure.

**Study design**—Cohort study; Level of evidence, 3.

**Methods**—A total of 110 consecutive patients underwent meniscal repair at our institution between August 1998 and July 2001. Three patients were lost to follow-up, and the remaining 107 (mean age, 15.9 ± 4.4 years) had a minimum 5-year follow-up (mean follow-up, 5.5 years). Thirty-two patients (30%) received ketorolac perioperatively. The primary outcome measure was reoperation for continued symptoms of meniscal pathology. Asymptomatic patients were evaluated by the International Knee Documentation Committee (IKDC) Subjective Knee Form, Short Form-36 (SF-36) Health Survey, and Knee Outcome Osteoarthritis Score (KOOS).

**Results**—Kaplan-Meier survivorship revealed no difference in reoperation rates with and without the administration of perioperative ketorolac ( $P = .95$ ). There was an overall failure rate of 35% (37/107 patients), with a 34% failure rate in patients receiving ketorolac (11/32 patients). Multivariable Cox regression confirmed that age, duration of symptoms, meniscal tear type, fixation technique, concurrent anterior cruciate ligament repair, and ketorolac usage did not have an impact on the rate of failure ( $P > .05$  for all; ketorolac use,  $P > .50$ ). Female sex ( $P = .04$ ) and medial location ( $P = .01$ ) were predictive of an increased risk for reoperation.

© The Author(s) 2014

This open-access article is published and distributed under the Creative Commons Attribution - NonCommercial - No Derivatives License (<http://creativecommons.org/licenses/by-nc-nd/3.0/>), which permits the noncommercial use, distribution, and reproduction of the article in any medium, provided the original author and source are credited. You may not alter, transform, or build upon this article without the permission of the Author(s). For reprints and permission queries, please visit SAGE's Web site at <http://www.sagepub.com/journalsPermissions.nav>.

<sup>†</sup>Address correspondence to Martha M. Murray, MD, Department of Orthopaedic Surgery, Children's Hospital of Boston, 300 Longwood Avenue, Boston, MA 02115, USA ([martha.murray@childrens.harvard.edu](mailto:martha.murray@childrens.harvard.edu)).

**Conclusion**—Failure of meniscal repair was not altered with the administration of perioperative ketorolac. Further work studying the effects of longer term anti-inflammatory use after meniscal repair is necessary before stating that this class of medications has no effect on meniscal healing.

**Clinical Relevance**—Results of this study suggest that nonsteroidal anti-inflammatory ketorolac can be administered perioperatively during a meniscal repair procedure to harness its benefits of decreased narcotic requirement, decreased pain, and shorter length of hospital stay without negatively influencing the long-term outcome of the surgery.

## Keywords

meniscus; meniscal repair; NSAID; ketorolac

There has been recent interest on the effect of nonsteroidal anti-inflammatory medications on bone and soft tissue healing. While the administration of nonsteroidal anti-inflammatory drugs (NSAIDs) after orthopaedic surgery is attractive because of their analgesic and anti-inflammatory effects,<sup>46</sup> the administration of these drugs remains controversial because of conflicting results of various studies. Some have demonstrated that NSAIDs can have a negative effect on fracture<sup>12,13,24</sup> and soft tissue healing.<sup>13,18</sup> For certain NSAIDs like indomethacin, the state of evidence in the literature for the detrimental effect on both bone healing and soft tissue healing is strong.<sup>12,13,18</sup> The effect of anti-inflammatory medications on healing is likely dependent on the time of administration, model chosen for study, and dosing,<sup>48</sup> factors that likely contribute to the variable results reported in vitro and in vivo for bone and ligament healing.<sup>12,13,35</sup> However, the effect of other NSAIDs such as ketorolac on tissue healing is not as definite.<sup>23-25,34,35</sup> While postoperative ketorolac administration in adult spinal fusion patients led to a higher rate of nonunions, bone healing does not seem to be impaired in young patients<sup>34,35</sup> and after brief postoperative administration (<7 days)<sup>23</sup> of ketorolac. The influence of ketorolac on soft tissue healing is not well explored however, and to our knowledge, no studies have evaluated the effect of these medications on meniscal healing.

Meniscal function is important as it acts as a load bearer and shock absorber in the tibiofemoral joint by increasing the surface for load transmission,<sup>5,39</sup> has proprioceptive function, stabilizes the knee, and aids to the lubrication and nutrition of the articular cartilage.<sup>30,41,42,47,58</sup> Thus, there is great interest in meniscal preservation procedures including meniscal repair because meniscectomy has been shown to significantly increase the peak load on the cartilage surfaces of the knee and subsequent development of osteoarthritis.<sup>42</sup> Past reports have shown that arthroscopically repaired menisci have the potential for long-term success both clinically and radiographically.<sup>32,33</sup> A recent meta-analysis comparing the clinical outcomes in randomized prospective studies between meniscectomy and meniscal repair showed significantly better results after the repair.<sup>57</sup> Repair leading to a functional meniscus does not only improve clinical symptoms compared with a meniscus-insufficient knee but also significantly delays radiographic signs of osteoarthritis in the knee.<sup>52</sup> Therefore, preservation of the meniscus is desirable to preserve the integrity of the articular cartilage whenever possible.

The success of meniscal repair is largely judged by the clinical outcome or absence of symptoms because routine conventional magnetic resonance imaging (MRI) as the standard noninvasive method for the evaluation of meniscal pathology is difficult to analyze after meniscal repair.<sup>14,54</sup> This is because of the enduring increased signal intensity after the repair, which can be elevated for more than 13 years postoperatively<sup>44,54</sup> and complicates the differentiation between scar tissue and re-tear. In this case, the more invasive method of direct or indirect magnetic resonance arthrography shows a higher sensitivity and specificity in detecting a failed meniscal repair.<sup>14</sup>

Meniscal repair outcome studies at greater than 5 years have shown a success rate of between 71% and 84%.<sup>38,44,45,49-51</sup> While the repair technique evolved from earlier all-open meniscal repairs<sup>44,49,50</sup> to less invasive all arthroscopic inside-out and all-inside meniscal repair techniques,<sup>38,45,51</sup> failure rates stayed at a constant level. Investigators previously reported that patient age,<sup>7</sup> time since injury,<sup>28</sup> complex tears,<sup>11</sup> and ligamentous instability<sup>4</sup> are risk factors for poor clinical outcome of meniscus repair; however, little is known about the effect of perioperative NSAID use.

Ketorolac is an NSAID with analgesic effects that can be administered intravenously, intramuscularly, and orally. Its usage in the perioperative period has been associated with several important patient benefits, including decreased narcotic requirement,<sup>1,3</sup> reduction of postoperative nausea and vomiting,<sup>21</sup> decreased pain,<sup>3,15,40,55</sup> and shorter length of hospital stay.<sup>15,19</sup> In this study, we wished to determine if these benefits of ketorolac use were also associated with increased risk of meniscal repair failure. To begin to address this question, a retrospective study was performed to determine if the use of a common anti-inflammatory medication at a common dose, either in the operating room or postoperative anesthesia care unit, had any significant effect on the rate of failure of meniscal repair as measured by return to surgery for recurrent meniscal symptoms.

## METHODS

### Study Design

A retrospective review of 110 patients undergoing meniscal repair was performed after institutional review board approval was obtained. All patients who underwent meniscal repair for an arthroscopically visualized tear at our institution between August 1998 and July 2001 were included. A computer-based search of operative records of patients who had undergone a procedure for a meniscal repair identified this group of patients. Clinic and operative notes were reviewed for each patient's data. Three patients were lost to follow-up. Of the 107 patients included in our analysis, the mean age was 15.9 years. There were 62 (58%) women and 45 (42%) men in our study. The medial meniscus was repaired in 61 (57%) patients and the lateral meniscus in 46 (43%). Forty-three (40%) patients had a concurrent anterior cruciate ligament (ACL) reconstruction. Meniscal repairs were performed in an inside-out suture technique with nonabsorbable sutures in 8 cases (4 Prolene [polypropylene suture, Ethicon; Johnson & Johnson, New Brunswick, New Jersey, USA], 4 Ethibond [polyester suture, Ethicon]) and bioabsorbable sutures in 30 cases (Ethicon PDS [polydioxanone] suture), using an entirely arthroscopic implantation of all inside devices in 54 cases (16 DePuy Mitek Tophat [DePuy Mitek, Raynham, Massachusetts, USA], 19

DePuy Clearfix Meniscal Screw, 19 DePuy RapidLoc Suture Arrows) or both in 15 cases. Thirty-two patients (30%) received ketorolac either intraoperatively or in the acute postoperative period (ie, in the postanesthesia care unit). Ketorolac dose was adjusted to the patient's body weight (range, 7.5-60 mg). This group of patients was compared with 75 patients (70%) who did not receive anti-inflammatory medications in the perioperative setting.

Age, sex, type of meniscal tear, duration of symptoms, fixation technique, medial or lateral location of defect, concurrent ACL repair, and length of follow-up were recorded for each patient. Continuous variables were categorized as follows: time prior to fixation was 3 months; fixation techniques were grouped either as implants, suture repair, or a combination of both techniques; concurrent ACL reconstruction was recorded if performed during the same procedure; and tear type was grouped as either peripheral (which included peripheral and capsular bucket handle tears) or central (which included longitudinal tears in the red-white zone as well as horizontal tears). Seven discoid meniscal tears were classified based on the location of the tear within the meniscus, with 6 of these tears located peripherally and 1 located in the red-white zone. The primary outcome measure was reoperation for continued symptoms of meniscal pathology, indicative of a failed repair.

Attempts were made to contact all 70 asymptomatic patients. Internet search engines and telephone directory assistance were used to locate former patients whose addresses were not current. Twelve of the 70 asymptomatic patients could not be located in 2005 and were considered lost to follow-up.

Subjects completed a 15- to 20-minute telephone interview. The Knee Injury and Osteoarthritis Outcome Score (KOOS), Short Form-36 (SF-36) Health Survey, and International Knee Documentation Committee (IKDC) Subjective Knee Form were administered.

The KOOS assesses symptoms, pain, activities of daily living (ADLs) function, sports/recreation, and quality of life. The SF-36 is a 36-question survey used to assess general health. The IKDC Subjective Knee Evaluation form assesses knee function and symptoms.

## Statistical Analysis

An initial power analysis was performed in planning this study. Since the primary efficacy analysis was aimed at comparing reoperation rates and Kaplan-Meier time to re-operation between patients who received ketorolac versus those who did not, we based our sample size requirements on the log-rank test for comparing survivorship curves (ie, freedom from meniscal reoperation) between the 2 groups. The power analysis indicated that a minimum sample size of 32 patients receiving ketorolac and not receiving ketorolac would provide 80% power to detect a moderate hazard ratio of 3.0 in the time to reoperation provided that a minimum of 30 meniscal reoperations occurred. Power analysis was performed using nQuery Advisor software (version 7.0; Statistical Solutions, Saugus, Massachusetts, USA). Patients receiving ( $n = 32$ ) and not receiving ( $n = 70$ ) ketorolac were compared on each of 8 variables to establish that the 2 groups were comparable with no confounding factors or imbalances. The Pearson chi-square or Fisher exact test for binary proportions were used to

assess differences in sex, duration of symptoms, type of meniscal tear, fixation technique, location of defect, concurrent ACL repair, and reoperation. Age was compared by the 2-sample Student *t* test. Similarly, we assessed differences between the 2 outcome groups: patients who had a reoperation due to continued symptoms of meniscal pathology ( $n = 37$ ) and those who remained asymptomatic ( $n = 70$ ). Survivorship was determined according to the Kaplan-Meier product-limit method and was used to ascertain whether the perioperative use of ketorolac was associated with earlier failures with the 2 groups compared by the log-rank test.<sup>31</sup> The Greenwood formula was used to calculate 95% confidence intervals at 1-year follow-up time points around the survivorship curves.<sup>29</sup> Other covariates were tested using the Cox multivariable proportional hazards regression model to assess their influence on the failure rate and control for possible confounding.<sup>56</sup> The hazard ratio<sup>19</sup> and 95% confidence intervals were calculated for significant independent predictors of meniscal reoperation. Fifty-eight of 70 asymptomatic patients were evaluated 5 years after surgery using 3 functional assessment instruments: KOOS, IKDC, and SF-36. The Mann-Whitney *U* test was used to assess differences in functional outcome scores between men and women. Two-tailed  $P < .05$  was considered the criterion for statistical significance. Analysis of the data was performed using the SPSS statistical package (version 16.0; SPSS Inc, Chicago, Illinois, USA).

## RESULTS

No differences were found according to ketorolac usage in any of the patient or surgical variables evaluated ( $P > .50$ ) (Table 1). Of the 37 patients having a reoperation due to recurrent meniscal symptoms, 30% had ketorolac usage, which was comparable to the 30% ketorolac usage among the 70 asymptomatic patients ( $P = .99$ ). There were no significant differences in the rates of reoperation with administration of perioperative ketorolac compared with the group not receiving ketorolac (11/32 patients [34%] vs 26/70 patients [37%];  $P = .99$ ) (Figure 1). Univariate analysis indicated no significant associations between meniscal reoperation and age, sex, duration of symptoms, tear type, fixation technique, concurrent ACL repair, or ketorolac usage ( $P > .10$  for all) (Table 2). A higher percentage of patients with medial location of the defect had a meniscal re-operation compared to lateral injuries (44% vs 22%;  $P = .02$ ).

Kaplan-Meier analysis indicated no significant difference in the time to meniscal reoperation between patients receiving and those not receiving ketorolac perioperatively ( $P = .95$ , log-rank test), as depicted by overlapping survivorship curves (Figure 2). At 5 years of follow-up, the 2 survivorship curves indicated that approximately 70% of patients were free from meniscal reoperation regardless of ketorolac usage, indicating that NSAID usage was not associated with earlier repair failures.

The multivariable Cox regression model indicated that age, duration of symptoms, meniscal tear type, fixation technique, concurrent ACL reconstruction, and ketorolac usage were not found to influence the rate of reoperation ( $P > .05$  for all). Female sex (hazard ratio = 2.1,  $P = .04$ ) and medial compared to lateral location of the defect (hazard ratio = 2.5,  $P = .01$ ) were found to be significant multivariate predictors of an earlier meniscal reoperation independent of age, duration of symptoms, tear type (peripheral vs central), fixation

technique, concurrent ACL repair, and ketorolac usage. The estimated monthly risk of meniscal reoperation is 2.1 times higher for women than men and 2.5 times higher for medial compared with lateral injuries (Table 3).

Functional outcome scores were obtained on 58 of 70 patients (83%) who did not have a meniscal reoperation (31 women and 27 men). Multiple regression analysis was used to determine which patient factors were associated with differences in total KOOS and subscores, total SF-36, and the IKDC Subjective Knee Evaluation Form. The only variable that demonstrated a significant association with these outcome scores was sex, with women having lower median scores than men on some outcome measures. Women had significantly lower scores at 5-year follow-up in KOOS subscores, including pain ( $P = .05$ ), ADL function ( $P < .01$ ), sports/recreation ( $P < .01$ ), and quality of life ( $P = .04$ ). No differences between sexes were observed for total KOOS ( $P = .34$ ) or total SF-36 ( $P = .32$ ), although over all IKDC scores were significantly lower in women ( $P < .01$ ).

## DISCUSSION

Failure of meniscal repair was not altered with the administration of perioperative ketorolac. This suggests that use of this medication in the early postoperative period may be selected for the advantages of decreasing patient pain without concern for substantial compromise of overall clinical success. Ketorolac has been shown to be an effective adjuvant for pain relief<sup>1,3,40,55</sup> and decreased narcotic use<sup>3,15</sup> in the postoperative setting. Literature regarding the effects of anti-inflammatory medications on connective tissue healing is full of seemingly controversial findings because of differences in models and study designs.<sup>15</sup> To our knowledge, no reports on the effects of anti-inflammatory medications on meniscal repairs have been conducted. In this study, the effects on meniscal repair of a common anti-inflammatory medication as it is clinically used (with respect to standard dose and time of administration) were measured.

There are several limitations to our study. First, our monitoring of anti-inflammatory medication was only documented in the perioperative period, either during surgery or in the postanesthesia care unit. There was no recording of NSAID use after discharge. Therefore, patients in either group may have had significantly different patterns of NSAID use after the first 12 hours after surgery. Second, our endpoint for patient follow-up ended with persistent symptoms requiring reoperation or resolution of symptoms. Our primary question was whether anti-inflammatory medications administered in the perioperative period had a significant effect on meniscal repair outcomes. Our primary outcome measure for patient follow-up was either repair survival until 5 years after surgery or reoperation at any time point up to 5 years after repair. Our secondary outcome measures were the KOOS, SF-36, and IKDC scores for patients who had not required repeat surgery. As the patients who had undergone reoperation had already failed by the primary outcome measure, they were not evaluated as part of the group that had not failed. All failures were symptomatic. Patients determined to have had a successful outcome were asymptomatic at the latest follow-up. Our study shows that these patients continued to do well. We assumed clinical success in patients with continued resolution of symptoms after surgery. However, recent work has suggested that reported clinical failure rates may underestimate the true wound healing



failure rates for meniscus, and that even in asymptomatic patients (clinical successes), the meniscus may have failed to heal in as many as 45% of cases.<sup>53</sup> Nevertheless, while one would not anticipate large differences in asymptomatic failures between the patients receiving ketorolac and those not receiving the medication, the true failure rate is more likely higher in both groups than that reported here.

In addition, there are distinct disadvantages in performing a cross-sectional retrospective study. One limitation is that it is difficult to ascertain that ketorolac as an intervention had any direct role in the outcome of meniscal repairs. This weaker evidence of true causality is a limitation. Despite this, a retrospective study of this type is a necessary step to effectively perform a prospective study. The lack of randomization of ketorolac use could have also increased the possibility of confounding, which is common in retrospective studies. However, Table 1 indicates no significant imbalances that would have created a bias when comparing meniscal reoperation rates between the 2 groups. Furthermore, multivariable analysis was applied to control for any possible selection bias in comparing re-operation rates for patients who received ketorolac perioperatively and those who did not.

This retrospective study was performed after all surgeries were completed, thus minimizing the ability of the surgeon to bias the results. In addition, to minimize bias, we looked at a series of consecutive patients, including patients who underwent meniscal repair before ketorolac was available. After ketorolac was available at our institution, it was almost universally adopted for these patients. This likely explains the finding that there were no significant differences between the ketorolac and no ketorolac groups in terms of meniscal tear size, location, or repair type. Eighty-five percent of patients were operated on by 1 surgeon; the other 15% had their surgery completed by 2 other surgeons. Thus, the likely reason we did not observe any surgeon-specific effect was that the majority of cases were performed by 1 surgeon. Similarly, the optimal technique was chosen for each case and performed by an experienced specialist, thus minimizing the influence a different technique would have on the individual outcome.

Radiographic evaluation of healing after meniscal repair is limited. MRI of the meniscus, especially in young patients, has limited value.<sup>37</sup> In addition, it becomes very difficult to determine if the meniscus has healed, even with specialized MRI studies. Reports suggest that in 50% to 60% of patients, a grade III signal alteration was seen on the magnetic resonance images at long-term follow-up after arthroscopic meniscal repair.<sup>20,44</sup> MRI signal alterations in the meniscus are divided into 3 grades; grade I and II describe areas of increased signal intensity that do not extend to an articulating surface, whereas grade III lesions reach the meniscal surface. Grades I and II changes are not usually seen arthroscopically and do not represent meniscal tears. Grade III changes are meniscal tears.<sup>9</sup> MRI is an ideal diagnostic tool for confirming clinical diagnosis of meniscal tears, but its use in observing healing of a meniscal tear after repair is limited. Hence, there is no method available for noninvasively determining the histologic rate of healing in patients, and clinical outcomes remain the most logical outcome measure.

The failure rate of 35% is consistent with the previously reported failure rates of meniscal repairs. Long-term survival studies of both arthroscopic and open techniques of meniscal



repairs have reported successful healing rates of between 71% and 84% when the procedure was performed for unstable peripheral meniscal tears.<sup>38,44,45,49-51</sup> The institution the study was performed in cares primarily for young patients. As a result, there is a relatively aggressive approach to meniscal repair in these young patients. Complex tears, tears in the red-white zone, discoid menisci, and isolated meniscal tears are often treated with repair rather than resection, given the potential benefit of retention of meniscal tissue. This may be part of the explanation for the relatively high failure rate seen in both patient groups. Another factor may be the activity level of the patients in the postoperative period. Adolescent patients have an increased risk of ACL graft failure after ACL reconstruction, a finding that has been attributed to an increased activity level over other age groups.<sup>10</sup> It is possible that this same activity differential places the adolescent patients in this study at higher risk for meniscal repair failure as well. In this study, 22% of tears were not peripheral, longitudinal tears. This is different from prior studies in adult populations that have focused solely on repair of peripheral, long-itudinal tears.<sup>6,16,17,20</sup> These tear types are known to have improved repair results,<sup>4,27</sup> likely because of improved vascularity<sup>2</sup> and biology.<sup>43</sup> In addition, only 40% of the patients in this study had a concomitant ACL reconstruction, an additional factor known to improve meniscal healing results.<sup>22,26,36</sup> Prior studies have had higher rates of concomitant ACL reconstruction ranging from 58% to 72% of patients.<sup>8,22,26,36</sup> No significantly improved healing in the meniscal repair group with concomitant ACL reconstruction was found in our study. Thirty-seven percent of meniscal repairs with concomitant ACL reconstruction failed within 5 years, whereas only 33% of the meniscal repairs in the nonconcomitant ACL reconstruction group underwent reoperation. This is in contrast to multiple other studies that demonstrate a significant improvement in meniscal healing rate with ACL reconstruction. The reasons for the different finding in this outcome are unknown but may be because of the relatively small sample size of the knees with concomitant ACL reconstruction, thus providing low power to detect a difference between these groups.

In this study, the ketorolac and control groups were not significantly different regarding the covariates tested in Table 1, and given that the percentages of patients requiring meniscal reoperation were so similar (34% with perioperative ketorolac and 35% without ketorolac), it is unlikely that this negative result ( $P = .99$ , Fisher exact test;  $P = .95$ , log-rank test in Kaplan-Meier analysis) is due to a type II error or false negative result. Given the lack of covariate imbalances that might otherwise have created bias or confounding and the sufficient sample sizes for achieving more than 80% power given the sample sizes of cases and control, it is highly probable that the risk of meniscal reoperation is not significantly influenced by the administration of ketorolac.

## CONCLUSION

In summary, this study did not yield conclusive data to support the hypothesis of a negative effect of perioperative administration of ketorolac on the outcome of meniscal repair and therefore suggests that using ketorolac in the perioperative period does not have any detrimental effect on the clinical success of meniscal repair. Further work is required to determine the effect of long-term NSAID use on meniscal healing.

## Acknowledgments

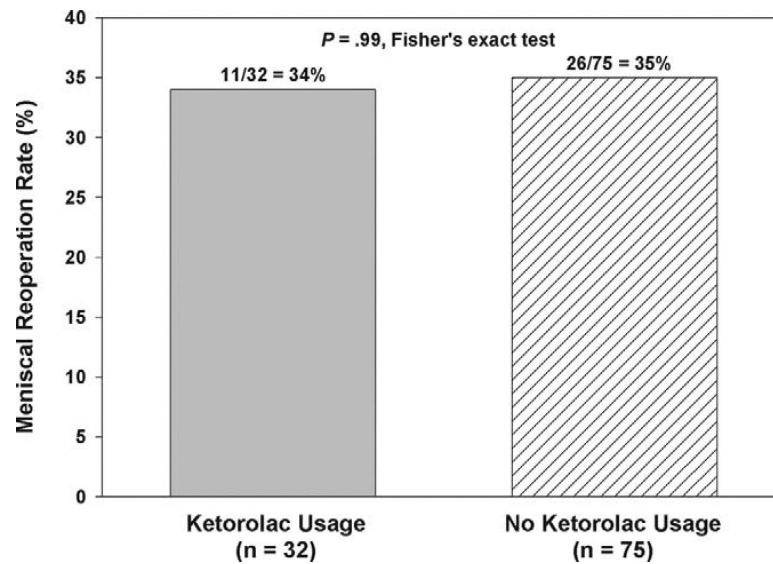
One or more of the authors has declared the following potential conflict of interest or source of funding: This study was funded by the Division of Sports Medicine, Boston Children's Hospital, and by the National Institute of Arthritis and Musculoskeletal and Skin Diseases, part of the National Institutes of Health, under Award Number 2R01-AR054099. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

## REFERENCES

1. Alexander R, El-Moalem HE, Gan TJ. Comparison of the morphine-sparing effects of diclofenac sodium and ketorolac tromethamine after major orthopedic surgery. *J Clin Anesth*. 2002; 14:187–192. [PubMed: 12031750]
2. Arnoczky SP, Warren RF. The microvasculature of the meniscus and its response to injury. An experimental study in the dog. *Am J Sports Med*. 1983; 11:131–141. [PubMed: 6688156]
3. Axelsson K, Gupta A, Johanson E, et al. Intraarticular administration of ketorolac, morphine, and ropivacaine combined with intraarticular patient-controlled regional analgesia for pain relief after shoulder surgery: a randomized, double-blind study. *Anesth Analg*. 2008; 106:328–333. [PubMed: 18165599]
4. Bach BR Jr, Dennis M, Balin J, Hayden J. Arthroscopic meniscal repair: analysis of treatment failures. *J Knee Surg*. 2005; 18:278–284. [PubMed: 16262009]
5. Baratz ME, Fu FH, Mengato R. Meniscal tears: the effect of meniscectomy and of repair on intraarticular contact areas and stress in the human knee. A preliminary report. *Am J Sports Med*. 1986; 14:270–275. [PubMed: 3755296]
6. Barber FA. Meniscus repair: results of an arthroscopic technique. *Arthroscopy*. 1987; 3:25–30. [PubMed: 3566892]
7. Barber FA, McGarry JE. Meniscal repair techniques. *Sports Med Arthrosc*. 2007; 15:199–207. [PubMed: 18004219]
8. Barrett GR, Field MH, Treacy SH, Ruff CG. Clinical results of meniscus repair in patients 40 years and older. *Arthroscopy*. 1998; 14:824–829. [PubMed: 9848593]
9. Behairy NH, Dorgham MA, Khaled SA. Accuracy of routine magnetic resonance imaging in meniscal and ligamentous injuries of the knee: comparison with arthroscopy. *Int Orthop*. 2009; 33:961–967. [PubMed: 18506445]
10. Borchers JR, Pedroza A, Kaeding C. Activity level and graft type as risk factors for anterior cruciate ligament graft failure: a case-control study. *Am J Sports Med*. 2009; 37:2362–2367. [PubMed: 19684294]
11. Boyd KT, Myers PT. Meniscus preservation; rationale, repair techniques and results. *Knee*. 2003; 10:1–11. [PubMed: 12649021]
12. Burd TA, Hughes MS, Anglen JO. Heterotopic ossification prophylaxis with indomethacin increases the risk of long-bone nonunion. *J Bone Joint Surg Br*. 2003; 85:700–705. [PubMed: 12892193]
13. Chen MR, Dragoo JL. The effect of nonsteroidal anti-inflammatory drugs on tissue healing. *Knee Surg Sports Traumatol Arthrosc*. 2013; 21:540–549. [PubMed: 22744434]
14. Ciliz D, Ciliz A, Elverici E, Sakman B, Yuksel E, Akbulut O. Evaluation of postoperative menisci with MR arthrography and routine conventional MRI. *Clin Imaging*. 2008; 32:212–219. [PubMed: 18502349]
15. De Oliveira GS Jr, Agarwal D, Benzon HT. Perioperative single dose ketorolac to prevent postoperative pain: a meta-analysis of randomized trials. *Anesth Analg*. 2012; 114:424–433. [PubMed: 21965355]
16. DeHaven KE, Arnoczky SP. Meniscus repair: basic science, indications for repair, and open repair. *Instr Course Lect*. 1994; 43:65–76. [PubMed: 9097138]
17. DeHaven KE, Black KP, Griffiths HJ. Open meniscus repair. Technique and two to nine year results. *Am J Sports Med*. 1989; 17:788–795. [PubMed: 2696377]

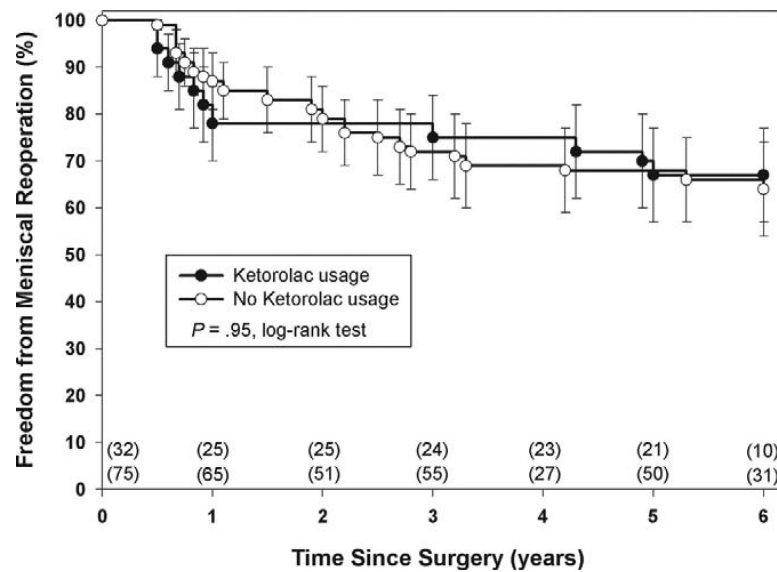
18. Dimmen S, Engebretsen L, Nordsletten L, Madsen JE. Negative effects of parecoxib and indomethacin on tendon healing: an experimental study in rats. *Knee Surg Sports Traumatol Arthrosc.* 2009; 17:835–839. [PubMed: 19296084]
19. Ebersson CP, Pacicca DM, Ehrlich MG. The role of ketorolac in decreasing length of stay and narcotic complications in the postoperative pediatric orthopaedic patient. *J Pediatr Orthop.* 1999; 19:688–692. [PubMed: 10488877]
20. Eggli S, Wegmuller H, Kosina J, Huckell C, Jakob RP. Long-term results of arthroscopic meniscal repair. An analysis of isolated tears. *Am J Sports Med.* 1995; 23:715–720. [PubMed: 8600740]
21. Fletcher D, Zetlaoui P, Monin S, Bombart M, Samii K. Influence of timing on the analgesic effect of intravenous ketorolac after orthopedic surgery. *Pain.* 1995; 61:291–297. [PubMed: 7659440]
22. Frosch KH, Fuchs M, Losch A, Sturmer KM. Repair of meniscal tears with the absorbable Clearfix screw: results after 1-3 years. *Arch Orthop Trauma Surg.* 2005; 125:585–591. [PubMed: 15645274]
23. Gerstenfeld LC, Al-Ghawas M, Alkhiary YM, et al. Selective and nonselective cyclooxygenase-2 inhibitors and experimental fracture-healing. Reversibility of effects after short-term treatment. *J Bone Joint Surg Am.* 2007; 89:114–125. [PubMed: 17200318]
24. Gerstenfeld LC, Thiede M, Seibert K, et al. Differential inhibition of fracture healing by non-selective and cyclooxygenase-2 selective non-steroidal anti-inflammatory drugs. *J Orthop Res.* 2003; 21:670–675. [PubMed: 12798067]
25. Glassman SD, Rose SM, Dimar JR, Puno RM, Campbell MJ, Johnson JR. The effect of postoperative nonsteroidal anti-inflammatory drug administration on spinal fusion. *Spine (Phila Pa 1976).* 1998; 23:834–838. [PubMed: 9563116]
26. Haas AL, Schepesis AA, Hornstein J, Edgar CM. Meniscal repair using the FasT-Fix all-inside meniscal repair device. *Arthroscopy.* 2005; 21:167–175. [PubMed: 15689865]
27. Hantes ME, Kotsovolos ES, Mastrokalos DS, Ammenwerth J, Paessler HH. Arthroscopic meniscal repair with an absorbable screw: results and surgical technique. *Knee Surg Sports Traumatol Arthrosc.* 2005; 13:273–279. [PubMed: 15455198]
28. Harris B, Miller MD. Biomedical devices in meniscal repair. *Sports Med Arthrosc.* 2006; 14:120–128. [PubMed: 17135958]
29. Harris, E.; Albert, A. *Survivorship Analysis for Clinical Studies.* Marcel Dekker; New York, NY: 1991.
30. Hollis JM, Pearsall AW 4th, Niciforos PG. Change in meniscal strain with anterior cruciate ligament injury and after reconstruction. *Am J Sports Med.* 2000; 28:700–704. [PubMed: 11032228]
31. Hosmer, DW.; Lemeshow, S. *Applied Logistic Regression.* 2nd ed.. Wiley; New York, NY: 2000.
32. Johnson MJ, Lucas GL, Dusek JK, Henning CE. Isolated arthroscopic meniscal repair: a long-term outcome study (more than 10 years). *Am J Sports Med.* 1999; 27:44–49. [PubMed: 9934417]
33. Kalliakmanis A, Zourntos S, Bousgas D, Nikolaou P. Comparison of arthroscopic meniscal repair results using 3 different meniscal repair devices in anterior cruciate ligament reconstruction patients. *Arthroscopy.* 2008; 24:810–816. [PubMed: 18589270]
34. Kay RM, Directo MP, Leathers M, Myung K, Skaggs DL. Complications of ketorolac use in children undergoing operative fracture care. *J Pediatr Orthop.* 2010; 30:655–658. [PubMed: 20864848]
35. Kay RM, Leathers M, Directo MP, Myung K, Skaggs DL. Perioperative ketorolac use in children undergoing lower extremity osteotomies. *J Pediatr Orthop.* 2011; 31:783–786. [PubMed: 21926877]
36. Kocabay Y, Nyland J, Isbell WM, Caborn DN. Patient outcomes following T-Fix meniscal repair and a modifiable, progressive rehabilitation program, a retrospective study. *Arch Orthop Trauma Surg.* 2004; 124:592–596. [PubMed: 15071747]
37. Kocher MS, DiCanzio J, Zurakowski D, Micheli LJ. Diagnostic performance of clinical examination and selective magnetic resonance imaging in the evaluation of intraarticular knee disorders in children and adolescents. *Am J Sports Med.* 2001; 29:292–296. [PubMed: 11394597]

38. Majewski M, Stoll R, Widmer H, Muller W, Friederich NF. Midterm and long-term results after arthroscopic suture repair of isolated, longitudinal, vertical meniscal tears in stable knees. *Am J Sports Med.* 2006; 34:1072–1076. [PubMed: 16452267]
39. Maquet PG, Van de Berg AJ, Simonet JC. Femorotibial weight-bearing areas. Experimental determination. *J Bone Joint Surg Am.* 1975; 57:766–771. [PubMed: 1158911]
40. Matava MJ, Prickett WD, Khodamoradi S, Abe S, Garbutt J. Femoral nerve blockade as a preemptive anesthetic in patients undergoing anterior cruciate ligament reconstruction: a prospective, randomized, double-blinded, placebo-controlled study. *Am J Sports Med.* 2009; 37:78–86. [PubMed: 18936277]
41. McDermott I. Meniscal tears, repairs and replacement: their relevance to osteoarthritis of the knee. *Br J Sports Med.* 2011; 45:292–297. [PubMed: 21297172]
42. McDermott ID, Amis AA. The consequences of meniscectomy. *J Bone Joint Surg Br.* 2006; 88:1549–1556. [PubMed: 17159163]
43. Mesiha M, Zurakowski D, Soriano J, Nielson JH, Zarins B, Murray MM. Pathologic characteristics of the torn human meniscus. *Am J Sports Med.* 2007; 35:103–112. [PubMed: 17092929]
44. Muellner T, Egkher A, Nikolic A, Funovics M, Metz V. Open meniscal repair: clinical and magnetic resonance imaging findings after twelve years. *Am J Sports Med.* 1999; 27:16–20. [erratum. 1999;27:379]. [PubMed: 9934413]
45. Noyes FR, Chen RC, Barber-Westin SD, Potter HG. Greater than 10-year results of red-white longitudinal meniscal repairs in patients 20 years of age or younger. *Am J Sports Med.* 2011; 39:1008–1017. [PubMed: 21278428]
46. Parvizi J, Miller AG, Gandhi K. Multimodal pain management after total joint arthroplasty. *J Bone Joint Surg Am.* 2011; 93:1075–1084. [PubMed: 21655901]
47. Renstrom P, Johnson RJ. Anatomy and biomechanics of the menisci. *Clin Sports Med.* 1990; 9:523–538. [PubMed: 2199066]
48. Riew KD, Long J, Rhee J, et al. Time-dependent inhibitory effects of indomethacin on spinal fusion. *J Bone Joint Surg Am.* 2003; 85-A:632–634. [PubMed: 12672837]
49. Rockborn P, Messner K. Long-term results of meniscus repair and meniscectomy: a 13-year functional and radiographic follow-up study. *Knee Surg Sports Traumatol Arthrosc.* 2000; 8:2–10. [PubMed: 10663312]
50. Sommerlath K, Hamberg P. Healed meniscal tears in unstable knees. A long-term followup of seven years. *Am J Sports Med.* 1989; 17:161–163. [PubMed: 2757124]
51. Steenbrugge F, Verdonk R, Hurel C, Verstraete K. Arthroscopic meniscus repair: inside-out technique vs. Biofix meniscus arrow. *Knee Surg Sports Traumatol Arthrosc.* 2004; 12:43–49. [PubMed: 14513212]
52. Stein T, Mehling AP, Welsch F, von Eisenhart-Rothe R, Jager A. Long-term outcome after arthroscopic meniscal repair versus arthroscopic partial meniscectomy for traumatic meniscal tears. *Am J Sports Med.* 2010; 38:1542–1548. [PubMed: 20551284]
53. van Trommel MF, Simonian PT, Potter HG, Wickiewicz TL. Different regional healing rates with the outside-in technique for meniscal repair. *Am J Sports Med.* 1998; 26:446–452. [PubMed: 9617412]
54. Vance K, Meredick R, Schweitzer ME, Lubowitz JH. Magnetic resonance imaging of the postoperative meniscus. *Arthroscopy.* 2009; 25:522–530. [PubMed: 19409311]
55. Vintar N, Rawal N, Veselko M. Intraarticular patient-controlled regional anesthesia after arthroscopically assisted anterior cruciate ligament reconstruction: ropivacaine/morphine/ketorolac versus ropivacaine/morphine. *Anesth Analg.* 2005; 101:573–578. [PubMed: 16037178]
56. Vittinghoff, E.; Glidden, D.; Shiboski, S.; McCulloch, C. *Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models.* Springer; New York, NY: 2005.
57. Xu C, Zhao J. A meta-analysis comparing meniscal repair with meniscectomy in the treatment of meniscal tears: the more meniscus, the better outcome? [published online May 14, 2013]. *Knee Surg Sports Traumatol Arthrosc.* doi:10.1007/s00167-013-2528-6.
58. Zimny ML, Albright DJ, Dabezies E. Mechanoreceptors in the human medial meniscus. *Acta Anat (Basel).* 1988; 133:35–40. [PubMed: 3213403]



**Figure 1.**

Comparison of meniscal repair reoperation rates for patients receiving and not receiving perioperative ketorolac. Eleven of 32 (34%) patients receiving perioperative ketorolac required a reoperation due to recurrent meniscal symptoms, compared with 26 of 75 (35%) patients in the no ketorolac group. These rates were not significantly different between the 2 study groups by univariate analysis ( $P = .33$ , Fisher exact test). Multivariate logistic regression analysis confirmed that use of ketorolac was not a predictor of reoperation ( $P = .89$ ).



**Figure 2.**

Kaplan-Meier survivorship curves according to peri-operative usage of ketorolac with no significant difference between the 2 study groups ( $P = .95$ , log-rank test). No differences were detected between the 2 groups in the rate of meniscal reoperations. The error bars around the curves denote 95% confidence intervals as determined by the Greenwood formula. Numbers in parentheses along the x-axis represent patients in the ketorolac group (top row) and no ketorolac group (bottom row) with follow-up to that time point who were asymptomatic and had not undergone meniscal reoperation. The 2 groups started with 32 and 75 patients, respectively. At 5 years after surgery, there were 21 patients in the ketorolac group and 50 in the no ketorolac group with follow-up still free from meniscal reoperation.



TABLE 1

Characteristics of Patients in the 2 Study Groups<sup>a</sup>

Characteristic	Ketorolac Group (n = 32)	No Ketorolac Control Group (n = 75)	<i>P</i> <sup>b</sup>
Age, y, mean ± SD	15.8 ± 3.0	16.0 ± 4.9	.78
Sex			.83
Female	18 (29)	44 (71)	
Male	14 (31)	31 (69)	
Duration of symptoms <sup>c</sup>			.82
3 mo	18 (34)	35 (66)	
>3 mo	14 (30)	32 (70)	
Tear type <sup>c</sup>			.80
Peripheral	25 (34)	48 (66)	
Central	7 (29)	17 (71)	
Fixation technique			.90
Bioabsorbable suture	10 (33)	20 (67)	
Implant	15 (28)	39 (72)	
Both	4 (27)	11 (73)	
Nonabsorbable suture	3 (37)	5 (63)	
Location of defect			.83
Lateral meniscus	13 (28)	33 (72)	
Medial meniscus	19 (31)	42 (69)	
Concurrent ACL repair			.52
Yes	11 (26)	32 (74)	
No	21 (33)	43 (67)	
Reoperation due to recurrent meniscal symptoms			.99
Yes	11 (30)	26 (70)	
No	21 (30)	49 (70)	

<sup>a</sup>Values are presented as number of patients (%) unless otherwise indicated. Percentages are calculated horizontally and rounded to the nearest integer. ACL, anterior cruciate ligament; SD, standard deviation.

<sup>b</sup>Fisher exact test or chi-square test was used to compare proportions between study groups.

<sup>c</sup>Based on the total number of patients in each group with available data.

TABLE 2

Univariate Analysis: Comparison of Patients Who Underwent Reoperation due to Recurrent Meniscal Symptoms and Those Who Were Asymptomatic<sup>a</sup>

Characteristic	Meniscal Reoperation (n = 37)	Asymptomatic, No Reoperation (n = 70)	<i>p</i> <sup>b</sup>
Age, y, mean ± SD	16.6 ± 4.6	15.7 ± 4.4	.30
Sex			.31
Female	24 (39)	38 (61)	
Male	13 (29)	32 (71)	
Duration of symptoms <sup>c</sup>			.14
3 mo	15 (28)	38 (72)	
>3 mo	20 (44)	26 (56)	
Tear type <sup>c</sup>			.63
Peripheral	26 (36)	47 (64)	
Central	10 (42)	14 (58)	
Fixation technique			.40
Bioabsorbable suture	10 (33)	20 (67)	
Implant	16 (30)	38 (70)	
Both	8 (53)	7 (47)	
Nonabsorbable suture	3 (38)	5 (62)	
Location of defect			.02 <sup>d</sup>
Lateral meniscus	10 (22)	36 (78)	
Medial meniscus	27 (44)	34 (56)	
Concurrent ACL repair			.68
Yes	16 (37)	27 (63)	
No	21 (33)	43 (67)	
Ketorolac perioperative usage			.99
Yes	11 (34)	21 (66)	
No	26 (35)	49 (65)	

<sup>a</sup>Values are presented as number of patients (%) unless otherwise indicated. Percentages are calculated horizontally and rounded to the nearest integer. ACL, anterior cruciate ligament; SD, standard deviation.

<sup>b</sup>Fisher exact test or chi-square test was used to compare proportions between study groups.

<sup>c</sup>Based on the total number of patients in each group with available data.

<sup>d</sup>Statistically significant ( $P < .05$ ).

**TABLE 3**Multivariate Cox Regression Analysis: Predictors of Meniscal Reoperation<sup>a</sup>

Variable	<i>P</i>	Hazard Ratio	95% CI
Age	.20		
Sex (female vs male)	.04 <sup>b</sup>	2.1	1.2-4.4
Duration of symptoms	.08		
Tear type	.59		
Fixation technique	.39		
Location (medial vs lateral)	.01 <sup>b</sup>	2.5	1.3-3.4
Concurrent ACL repair	.57		
Ketorolac perioperative usage	.89		

<sup>a</sup> ACL, anterior cruciate ligament; CI = confidence interval.<sup>b</sup> Significant independent predictor of meniscal reoperation.